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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR No. 0054793

MEMORANDUM

DATE: December 12, 2007

SUBJECT: **Cyprosulfamide:** Qualitative Risk Assessment Based On C57BL/6J Mouse Carcinogenicity Dietary Study

P.C. Code: 877400

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BACKGROUND

A carcinogenicity study in C57BL/6J mice was conducted by Bayer CropScience, Sophia Antipolis Cedex, France, for Bayer AG, Bayer CropScience, Monheim, Germany, and completed December 1, 2006 (Study No. SA 04065, MRID No. 47069818).

The study design originally allocated groups of 50 mice to dose levels of 0, 350, 2000 and 7000 ppm of Cyprosulfamide for 80 weeks. An additional ten mice per sex per dose were designated for interim sacrifice at week 53. Since there was excessive mortality at the 7000 ppm dose group, an additional dose group of 3500 ppm was added one month after the start of the study and all 7000 ppm dose group animals were terminated (females at week 6 and males at week 46). Final dosing levels were

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equivalent to 0, 50, 287 and 506 mg/kg/day for males and 0, 63, 354 and 616 mg/kg/day for females. There were no compound-related tumors in the males so only the analyses of the females are presented in this document.

ANALYSES

Survival Analyses

There were no statistically significant incremental changes in mortality with increasing doses of Cyprosulfamide in female mice (Table 1).

Tumor Analyses

Female mice had a statistically significant trend at $p < 0.01$, and a significant pair-wise comparison of the 3500 ppm dose group with the controls at $p < 0.05$, for histiocytic sarcomas. The statistical analyses of the tumors in the female mice were based upon Fisher's Exact Test for pair-wise comparisons and the Exact Test for trend (Table 2).

Table 1. Cyprosulfamide – C57BL/6J Mouse Study (MRID 47069818)

Female Mortality Rates[+] and Cox or Generalized K/W Test Results

	Weeks				
Dose (ppm)	1-26	27-52	53[i]	53-81[f]	Total
0	1/60	5/59	10/54	4/44	10/50 (20)
350	2/60	2/58	9/56	4/47	8/51 (16)
2000	2/58[a]	7/56	7/49	4/42	13/51 (25)
3500	0/60	2/60	10/58	9/48	11/50 (22)

[+]Number of animals that died during interval/Number of animals alive at the beginning of the interval.

[i]Interim sacrifice at week 53.
[f]Final sacrifice at weeks 79-81.

[a]Two accidental deaths, one each at weeks 2 and 26, dose 2000 ppm.

( )Percent.

Note: Time intervals were selected for display purposes only.
Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

Table 2. Cyprosulfamide – C57BL/6J Mouse Study (MRID 47069818)

Female Histiocytic Sarcoma Tumor Rates[+]
and Fisher's Exact Test and Exact Test for Trend Results

	Dose (ppm)			
	0	350	2000	3500
Histiocytic Sarcomas (%)	0/44 (0)	1/47 (2)	0/42 (0)	5[a]/48 (10)
p =	0.007396**	0.51648	1.0000	0.03482*

+Number of tumor bearing animals/Number of animals examined, excluding those that died or were sacrificed before week 54.

[a]First histiocytic sarcoma observed at week 62, dose 3500 ppm.

Note: Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

References

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